International Journal of Ophthalmic Research

Online Submissions: http://www.ghrnet.org/index./ijor/
doi:10.17554/j.issn.2409-5680.2017.03.58

Int. J. Ophthalmic Res 2017 March; 3(1): 214-216
ISSN 2409-5680

ORIGINAL ARTICLE

Low-dose Topical Mitomycin-C in the Treatment of Severe Vernal Keratoconjunctivitis

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Conflict-of-interest statement: The author(s) declare(s) that there is no conflict of interest regarding the publication of this paper.

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Received: January 12, 2017
Revised: February 18, 2017
Accepted: February 20, 2017
Published online: March 25, 2017

ABSTRACT

BACKGROUND: Corticosteroids and mast–cell stabilizers are commonly used in treatment of vernal keratoconjunctivitis (V.K.C), but regarding the side – effects of the agents and poor response in severe cases, the aim of this study was to investigate the effect of low dose topical mitomycin- c 0.01% in the treatment of severe vernal keratoconjunctivitis.

METHODS: In a double blind randomized clinical trial, 40 patients with V.K.C were randomly assigned to two equal size groups. One group received topical 0.01% Mitomycin-C and another group received placebo. Complaints (tearing, itching, and mucosal discharge) and symptoms (papillae, Micropannus, hyper injection, corneal and limbus involvement) were assessed at the baseline and 2 weeks after treatment in two groups. Data were analyzed by statistical methods in SPSS.16.

RESULT: 40 patients were studied including 31 male and 9 female with average of 14.7 ± 3.8 years in case group and 16.2 ± 8.4 in control group. The mean disease duration in case group was 3.5 ± 3.2 years and in control group was 15 ± 4.6. Comparing the severity of complaints and symptoms two weeks after treatment in two groups, there was a statistically significant difference in the tearing (p = 0.029) and the size of papillae (p = 0.006). There wasn't significant difference on other complaints and symptoms between two groups and no adverse effects of treatment with Mitomycin-C were observed.

CONCLUSION: This study showed that use of topical mitomycin-C 0.01% along with usual routine drugs reduces the severity of tearing and the size of papillae and it may be considered as a conventional treatment on patients with severe V.K.C.

Key words: Vernal keratoconjunctivitis; Mitomycin-C; Mast–cell stabilizers

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Ojaghi H, Masoumi R, Notaraj H. Low-dose Topical Mitomycin-C in the Treatment of Severe Vernal Keratoconjunctivitis. *International Journal of Ophthalmic Research* 2017; 3(1): 214-216 Available from: URL: http: //www.ghrnet.org/index.php/ijor/article/view/1965

INTRODUCTION

Seasonal conjunctivitis is the most severe form of allergic conjunctivitis which is mostly seen in young men. The main immunological mechanism is unknown[1-2]. The prevalence of vernal keratoconjunctivitis (V.K.C) in a study conducted by Leonard *et al*. was estimated as 7.8 per 100,000 that was more prevalent among young men than young women[3].

Sacchetti and *et al* in a study stated that the quality of life in children can be directly correlated with the prevalence of V.K.C in them[4]. Also Kumar *et al*. discussed about new therapeutic approaches for the management of vernal keratoconjunctivitis in children[5]. The disease is usually self-limiting but sometimes they are more serious and their control is difficult. If the symptoms are not limited by themselves or cause pain to the patient, medicine is prescribed that include mast cell stabilizers and steroids. Symptoms

can be seen in all seasons, but are more intense in spring and summer[6]. Corneal complications are often problematic for people suffering from the disease. A group of drugs that are commonly used to treat the disease are corticosteroids and mast cell stabilizers that steroids lead to many complications such as cataracts, glaucoma, increased intraocular pressure, infection and others. Therefore using an alternative, effective and safe medicine to control the disease can greatly reduce complications and blindness caused by the complications of the disease.

VKC is a disease showing great racial and geographical variation. It is most common and most severe in hot, arid environments such as the Mediterranean basin, West Africa, and the Indian subcontinent. Patients with VKC generally present in early to mid-childhood. Patients from age 1 to 22 years old (mean 6 ± 3.7 years) may present with signs and symptoms of VKC[7].

Mitomycin C is used to inhibit the cell proliferation and in addition to its usage in pterygium and glaucoma surgery, it has been used in the treatment of many patients with conjunctiva and corneal epithelium cancers[8-13]. The aim of this study was to evaluate the effect of mitomycin-C 0/01% in treatment of severe resistant to treatment V.K.C.

METHODS

This is a double blind clinical trial study that was conducted on 40 patients with resistant to treatment V.K.C. Inclusion criteria were: no corneal epithelial defects, lack of eye disease and exclusion criteria were increasing the severity of the disease and side effects during the study period. Characteristics of complaints (itching, tearing and eye discharge) and signs (corneal involvement, micropannus, edemalimbus, papilla, and the congestion) of the disease were measured by clinical examinations and entered in checklists before, during and after study periods. It should be noted that the rater was not familiar with the classification of the groups. The case group treated with low dose topical mitomycin-c along with other eye drops such as Nephazoline, Antazoline,betamethasone and Cromolyn. In the control group over a period of two weeks, normal saline was used as placebo along with other eye-drops. The collected data were analyzed using statistical methods in SPSS.16.

RESULT

SOf all patients, 31 (77.5%) were male and 9 (22.5%) were female. The mean age of the case group and control group was 13.8 ± 2.7 and 8.4 ± 3.2, respectively. The mean duration of illness in case group patients was 3.2 ± 3.5 years and in control group patients was 4.5 ± 4.6. Of all patients, 7 (17.5%) had a history of seasonal allergy and allergic which 4 patients (57.1%) in the control group and 3(42.9%) in case group. Of all patients, 4(10%) had a positive family history. All studied patients complained of itching and most of them (34 patients) had high level (severe, very severe) of itching. After completing the course of treatment, significant improvement was observed in both case and control groups. (p = 0.001) In the case group, 1 patient and in the control group 4 patients complained about intense itching after two weeks. By clinically examination we showed that, 100% of patients in the case group and 95% of patients in the control group had medium to high degrees of eye congestion before entering the study. At the end of the treatment in the case group, 80% of patients have mild degree of eye congestion and 20% had moderate to severe eye congestion. (p = 0.001) In the control group, after 2 weeks of using previous common drugs associated with normal saline, 45% of patients had mild, 45% moderate and 10% severe eye congestion degree, respectively, and eye congestion had not been completely cut off in none of the patients. (p = 0.045) Before treatment, 70 percent in the case group and 65 percent of patients in the control group had macro papilla. The Papilla size change rate in two groups was statistically significant difference after treatment. (p=0.006) Before treatment, 40% in the case group and 50% in the control group had no corneal involvement and the most prevalent type of involvement in each group was infiltration and Pigment epithelial detachment (PED), respectively, each with 30%. The difference was not significant between the two groups in terms of involvement. In the case group 25 % of patients and in the control group 35% of patients had micropannus before entering the study. After two weeks treatment, this rate declined to 5% in the case group and 15% in the control group, respectively and this reduction rate wasn't significant between two groups (Table 1).

DISCUSSION

The study showed a significant difference between the groups in terms of tearing so that improvement in the case group was significantly higher than the control group (p = 0.029). In Memarzadeh and Emad studies, tearing had a significant reduction after taking mitomycin-C[1,14]. In studies conducted in other places it was found that, compared to steroids, mitomycin-C wasn't more effective in tearing improvement[15-16].

The results of our study showed that the recovery rate and reduction the severity of itching in the patients of the case group was higher compared to the control group but was not statistically significant.However in the studies conducted in other places, the recovery rate and reduction of the severity of itching in the case group compared to the control group had significant difference[1,14].

Other examined complaint was the patients' eye discharge that there was no significant difference between the two groups but the rate of improvement was greater in the case group than control group. In a study conducted by Jain[16], mitomycin-c was better in improving three of the symptoms and complaints of V.K.C including eye discharge than steroids.

In this study, a significant difference (p = 0.006) was observed among the patients in terms of reducing the size of the papilla between the two groups before and after treatment. In studies done in other places, although most of the complaints and symptoms had decreased, but there was no difference between the two groups in terms of papilla size change[1,14].

In this study, by clinically examined we showed that reducing the severity of eye congestion (Ocular congestion) in patients who were

Table 1 Severity of complaints and symptoms in two groups before and after treatment.

Groups	Mitomycin-C (n = 20)		Placebo (n = 20)		p-value
	Before	After	Before	After	
Variables	n(%)	n(%)	n(%)	n(%)	
Complaints					
Tearing	18(90)	7(35)	18(90)	15(75)	0.029
Itching	20(100)	15(75)	20(100)	18(90)	1
Severe eye congestion	15(75)	1(5)	15(75)	2(10)	0.23
Discharge	14(70)	1(5)	14(70)	5(25)	1
Symptoms					
Limbal edema	8(40)	1(5)	7(35)	3(15)	0.74
Micropannus	5(25)	1(5)	7(35)	3(15)	0.49
Cornel involvement	12(60)	4(20)	10(50)	9(45)	0.29
Macro-papillae	14(70)	9(45)	13(65)	15(75)	0.006

treated with Mitomycin-C was higher than patients who were treated with normal saline but the difference was not statistically significant. In Jain's study, mitomycin-C has been reported as an effective drug in reducing the eye congestion in the treatment of severe V.K.C.

Other symptoms that were evaluated in this study in patients before and after treatment are: Corneal involvement, micropannus and limbal edema. In these cases in the case group compared to the control, a noticeable improvement of symptoms was observed but not significant.

In studies done in other places, the above mentioned symptoms had a remarkably good response to treatment with mitomycin-C[1,5,13-14]. Also in the study conducted by Jain and Akpek *et al*[16-17], limbal edema has been substantially improved with the use of mitomycin-C in comparison with steroids. The reason for the difference between the results of this study with the mentioned studies can be probably due to the small sample size in this study compared to other studies.

Kumar in a study showed that the Cyclosporine has been shown to be effective in the treatment of VKC but further randomized control trials are required to establish the minimum effective concentration[18].

Similar to our study, Al-Okour and *et al* in study showed that 72 (58.5%) of patients with VKC were males and average of 9.9 years. Severe vernal keratoconjunctivitis was seen in 31 (25.2%) patients: 16 (13%) patients of mixed type, 9 (7.3%) of limbal type, and 6 (4.9%) of palpebral type[19].

Mantelli *et al* showed that all topical drugs such as Mitomycin-c are effective in the treating acute phases of VKC and also showed significant improvement in all signs and symptoms, except photophobia in all groups which was in line with our study results[20].

CONCLUSION

The results showed that the use of topical mitomycin-C drop along with routine drugs significantly can be effective in reducing the size of the papilla and tearing. Also the use of topical mitomycin C compared to the drop of normal saline, tend to reduce complaints (ocular discharge and itching) and signs (hyperemia, limbal edema, corneal involvement and micropannus) in patients. Doing multi-center study in different parts of the country should be performed in future.

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Peer reviewer: Daoud Fahd